REMARKS

Reexamination and further and favorable reconsideration of the subject application in light of the following remarks are respectfully requested.

Initially, applicants gratefully acknowledge that the Examiner has clarified, on page 2 of the Office Action, that the claim status identified for claim 1 in the Amendment and Reply filed on December 3, 2003 should have recited "currently amended" as opposed to "original."

Turning now to the merits of the Office Action, the Examiner has rejected claims 1, 4-5, 7, 10-11, 13-16 and 18 under 35 U.S.C. § 102(b) as allegedly being anticipated by EP 0 636 363 ("EP '363"). Claims 1, 4-5, 7, 10-16 and 18 have also been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by JP 09 263579 ("JP '363"). Both of these rejections are respectfully traversed.

The Examiner has stated that the claimed mole percentages "appear" to fall within the same ranges as the "molar quantities" in EP '363 and the amounts in terms of "grams" in JP '579. Office Action at 3 & 4. The Examiner has also stated that the rejections "[would] be reconsidered" if applicants show that the molar quantities in EP '363 and the weights in grams in JP '579 do not correspond to the claimed mole percentages. Office Action at 3 & 4.

In EP '363, the examples describe a liposome using phosphatidyl choline (100 mM x 840 µl = 84 µmol), cholesterol (100 mM x 240 µl = 24 and µmol) and glucamine palmitate (10 Mm X 1200 µl = 12 µmol) as the film-constituent components (see Example 3). However, unlike applicants' claimed invention, there is no acidic compound specified which is used in the liposome.

In JP '579, the examples describe a liposome using N,N-dioctadecy-l2-(piperidine-4-il-oxy)acetamide (3 μM), cholesterol (6 μM) and dipalmitoylphosphatidylcholine (21 μM) as the film-constituent components (see Example 4); a liposome using N,N-dioctadecyl-2-(1-methylpiperidine-4-il-oxy)acetamide (3μM), cholesterol (6 μM) and dipalmitoylphosphatidylcholine (21 μm) as the film-constituent components (see Example 5); and a liposome using N,N-dioctadecyl-2-(1-dimethypiperidine-4-il-oxy)acetamide (3 μM), cholesterol (6 μM) and dipalmitoylphosphatidylcholine (21 μM) as the film-constituent components (see Example 6). However, like EP '363, JP '579 does not describe the use of an acidic compound as claimed in applicant's application. It should be noted that the amounts of the basic compounds used are not necessarily clear because the basic compounds used are expressed only by the concentration, not by the volume.

With regard to applicants' claimed invention, the molar ratios recited in independent claim 1, for instance, are a ratio of the basic compound to the total liposome constituents and a ratio of the acid compound to the total liposome constituents. Since neither EP '363 nor JP '579 describes an acidic compound a molar ratio of an acid compound to the total liposome constituents can not be made. Moreover, since the acid compound is part of the total liposome constituents neither the ratio of the basic compound to the total liposome constituents nor the ratio of the acid compound to the total liposome constituents can be calculated. Therefore, the Examiner's statement that the claimed molar ratios even appear to fall within the same ranges as the molar quantities in EP '363 and the amounts in terms of grams in JP '579 is not reasonable, nor possible. Since applicants have shown that the molar quantities in EP '363 and the weights in grams in JP '579 do not, as they

cannot, correspond to the claimed mole percentages, the rejections should not only be reconsidered, they should be withdrawn. The Examiner is therefore, respectfully requested to withdraw both of the above-mentioned rejections under 35 U.S.C. § 102(b).

The Examiner has also raised a number of rejections under 35 U.S.C. § 103(a) as follows:

(i) claims 1, 4-5, 7 and 10-18 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over EP '363;

(ii) claims 1-5, 7, and 10-19[1] have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over JP '363.

(iii) claims 8-9 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over EP '363 or JP '579 further in view of Gold (U.S. Patent No. 6,465,188); and

(iv) claims 6 and 12 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over EP '363 in combination with either Schneider (U.S. Patent No. 6,258,378) and Malone (PNAS, 86:6077-81 (1989)).

All four of these obviousness rejections are respectfully traversed.

According to the Examiner, "both EP ['363] and JP ['363] teach the targeted delivery of the drugs and both teach the presence of the claimed components and varying the amounts to obtain best possible delivery system is within the skill of the art and applicant has not shown any unexpected results using the broad claimed percentages." Office Action at 6.

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[1] It is noted that claim 19 was previously canceled and thus the rejection should not have included claim 19 in the listing of claims.

However, JP '579 merely describes the use of a specified piperidine derivative to improve the adhesion of a drug carrier to cells. EP '363 describes the use of a compound having a positively charged portion to improve the adhesion of a drug carrier to cells. To be more specific, EP '363 merely describes the use of a hydrophilic polymer compound on the surface of a drug carrier to improve the stability in blood of the drug carrier. In other words, in EP '363 and JP '579, the compound having a positively charged portion, the hydrophilic polymer compound and the specified piperidine derivative are important film-constituent components and the other compounds used as the film-constituent component may be those commonly used in the art and attract no particular interest.

Therefore, contrary to the Examiner's assertion, it is not within the skill of the artisan based on EP '363 and/or JP '579 to use the claimed basic compound and the claimed acidic compound in the specifically claimed amounts in order to promptly exhibit the target directive capability by a change in pH.

The comparison between Example 9 of the present application using the specified acidic compound and Comparative Example 7 of the present application using no specified acidic compound shows that there is a significant difference in the affinity for cells of the liposome at pH 6.0. This is clear from Fig. 4 and is a result one skilled in the art could not expect.

None of the other secondary references remedy the serious deficiencies of EP '363 and JP '579.

In view of the above, the claimed invention is not rendered obvious by the references cited by the Examiner. Therefore, withdrawal of all four rejections under 35 U.S.C. § 103(a) are respectfully requested.

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this Amendment and Reply or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

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By: _____
Susan M. Dadio
Registration No. 40,373

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620